

REMARKS

I. Status of the Claims

Claims 12-28 and 30 are now pending in this application. Claims 29 and 31 have been cancelled.

II. Allowable Subject Matter

Applicants thank the Examiner for indicating that claims 12-28 are allowed and claim 30 contains allowable subject matter. More specifically, the Examiner explains that the specification is enabling for the treatment of hypertension. Official Action of April 20, 2006, p. 2. In an effort to expedite prosecution, Applications have amended Claim 30 to recite a method of treating high blood pressure.

Applicants respectfully requests that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing all pending claims in condition for allowance.

Applicants respectfully submit that the proposed amendments do not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

III. Rejections under § 112, First Paragraph

The Examiner maintained his rejection of pending claims 29-31 under 35 U.S.C. § 112, first paragraph, asserting that the specification, while being enabling for the treatment of hypertension, diastolic dysfunction, and erectile dysfunction, does not reasonably provide enablement for a method of activating soluble guanylate cyclase (sGC) or a method of treating all other disorders of claim 30. Office Action at 2. The Examiner also alleged that claims 29 and 31 are “reach-through” claims because they “are drawn to ‘a method of activating soluble guanylate cyclase,’ without specifically identifying a disease state or condition....” *Id.* at 2-3.

Applicants respectfully disagree with these assertions. With respect to the arguments recited on page of 4 of the present Office Action, Applicants respectfully submit that the Examiner oversimplified the mechanisms of development and treatment of such disorders as atherosclerosis, thrombosis, diabetes, chronic liver insufficiency, and liver cirrhosis, among others. For example, the Examiner argued that thrombosis is not related to guanylate cyclase. Applicants respectfully submit, however, that it is well-known in the art that soluble guanylate cyclase (cGC), by increasing the level of cGMP and in turn activating cGMP-dependent protein Kinases, regulates platelet activation and aggregation, i.e., thrombosis. In fact, it has been clearly shown that nitric oxide, for example, inhibits platelet intravascular adhesion and aggregation through this exact cGC-mediated pathway. It necessarily follows, therefore, that thrombosis can be treated or prevented by regulating sGC.

Applicants also maintain that the Examiner oversimplified the pathophysiology of atherosclerosis, stating that it is “caused by plaques of cholesterol, lipids and cellular debris built up in the inner layer of the artery wall.” *Id.* at 4. While this is a generally

accurate description of histological changes that occur in atherosclerosis, it ignores the molecular mechanisms that underlie such events. It is well-established in the art that atherosclerosis, as well as changes in vascular smooth muscles associated with this disease, are associated with alterations in nitric oxide/cGC/cGMP/cGMP-dependent protein kinase signaling pathway. Therefore, atherosclerosis can be treated or prevented by activating sCG by administering the compounds of this invention.

Similarly, alterations in the nitric oxide/cGC/cGMP pathway have been shown in the art to occur in the setting of diabetes, cardiovascular disorders, endothelial dysfunction, angina pectoris, restenoses, myocardial infarct, strokes, cardiac insufficiency, bronchial asthma, chronic renal insufficiency, liver cirrhosis, restricted learning capacity or memory power, among other disorders.

Applicants thus respectfully maintain that the specification, in view of the level of knowledge and skill in the art, provides enablement for the method of treating or preventing all the disorders previously claimed. Applicants also respectfully disagree with the Examiner's interpretation of "reach-through" claims and thus maintain that the specification provides an adequate written description and enablement of claims 29 and 31.

In an effort to expedite the prosecution of the present application and allowance of the pending claims, however, Applicants cancel claims 29 and 31 and amend claim 30 without prejudice.

III. Conclusion

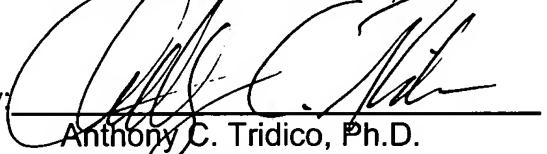
In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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By



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